

# Reaction field cavity optimization: A born-again Born model for ionic hydration

Chao-Ping Hsu

*Department of Chemistry, University of California at Berkeley, Berkeley, California 94720*

Martin Head-Gordon<sup>a)</sup>

*Department of Chemistry, University of California at Berkeley and Lawrence Berkeley National Laboratory, Berkeley, California 94720*

Teresa Head-Gordon<sup>a)</sup>

*Physical Biosciences and Life Sciences Divisions, Lawrence Berkeley National Laboratory, Berkeley, California 94720*

(Received 29 June 1999; accepted 8 September 1999)

We present a new quantum reaction field model, the electronic reaction field (ERF), which does not require the empirical specification of cavity shape and size. We demonstrate our approach on one of the simplest reaction field theories, the Born model for aqueous atomic ion solvation. The ERF model enforces complete solute–solvent separability so that the solute wave function is optimized under the boundary condition that it is fully contained within the cavity. This model imposes the exact condition necessary for treating the solute quantum mechanically and the other as a macroscopic classical dielectric, and allows the testing of the primary assumption in the dielectric continuum approximation that the molecular character of solvent is unimportant. We show that the Born theory for monovalent and divalent cations is consistent with ERF model enforcing full wave function containment, while strict solute–solvent separability gives a poor description for anions of any valency. © 1999 American Institute of Physics. [S0021-9606(99)51245-2]

## INTRODUCTION

Reaction field (RF) methods are one of the simplest approaches to modeling the condensed phase since only the solute is treated in microscopic detail.<sup>1</sup> Perhaps surprisingly, the results that have been obtained on a wide variety of molecular properties using reaction field descriptions of the condensed phase often mimic experiment quite closely. For example, chemical equilibria,<sup>2–4</sup> isomerization,<sup>5</sup> reactivity,<sup>6</sup> frequency shifts,<sup>7</sup> solubility data,<sup>8</sup> and higher order properties<sup>9</sup> have been predicted with RF models. This is very important because while the first fully quantum treatments of solvation are beginning to emerge, their cost is currently such that they will not be feasible for routine use in the near future.<sup>10,11</sup>

These results seem to indicate that RF approaches to solvation are of considerable value as a first approximation to the effects of the condensed phase when first-order electrostatic effects dominate. Recovery of additional nonelectrostatic or nonlinear free energy terms, such as the work to create a cavity of a given size, dielectric saturation, and electrostriction, are currently handled empirically in a RF model. These empirical approaches include adjusting cavity size, permitting the solute wave function to penetrate the cavity boundary to some degree, allowing the dielectric constant to change as a function of distance, or parametrizing these terms explicitly.<sup>12–23</sup> Therefore empirical adjustments or protocols to define the cavity shape and size are a sensible para-

metric means for compensating for a limited solvation model such as the reaction field when nonelectrostatic and/or nonlinear terms compete with linear-response electrostatics.

However, the purpose of our study is to clearly assess the extent to which success of reaction field modeling is attributable to it correctly describing the fundamental physics of solvation. We do this by lifting the empiricism of defining cavity size by treating the cavity extent as a variable that can be optimized. The electronic reaction field (ERF) model simultaneously varies the solute cavity radius and the quantum mechanical wave function of the solute in the presence of a reaction field, subject to the constraint that the solute wave function is entirely confined to the cavity.

The simplest reaction field model, the Born model,<sup>24</sup> treats the free energy of solvation for ions in solution according to the following process: (1) the ion is stripped of its charge in vacuum,  $\Delta G_1$ , (2) the uncharged sphere is transferred to a dielectric continuum, and gives rise to a free energy cost of creating a cavity,  $\Delta G_2$ , and (3) the sphere is recharged in the dielectric continuum solvent,  $\Delta G_3$ . In the original Born theory it was assumed that  $\Delta G_2$  is zero. Also Born theory assumes that there is no free energy change due to subsequent molecular reorganization of solvent around the recharged sphere, or nonlinear response terms, which we will call  $\Delta G_4$ . Therefore Born theory assumes that the free energy of solvation is due to the difference in charging in vacuum and dielectric

$$\Delta G_{\text{solvation}} = \Delta G_1 - \Delta G_3 = - \left( 1 - \frac{1}{\epsilon} \right) \frac{q^2}{2a}, \quad (1)$$

<sup>a)</sup>Authors to whom all correspondence should be addressed.

where  $\epsilon$  is a dielectric constant outside the sphere,  $q$  is the ionic charge, and  $a$  is the cavity radius. The Born model of the free energy of ion solvation is essentially a description of the dominance of the *electrostatic* free energy in the linear response regime.

In the ERF model, the constraint of a cavity confined wave function sets up a competition between reaction field stabilization, which favors smaller cavities, and the energetic cost, primarily through increased kinetic energy confining the molecular wave function, which favors larger cavities. Furthermore this model enforces *strict separability* of the solute and solvent charge densities, which is exactly the condition which is necessary as a basis for treating one quantum mechanically and the other as a macroscopic classical dielectric. Existing reaction field models do not enforce this constraint and must therefore be employed with empirically chosen cavities.<sup>25</sup> We find that this strict Born/ERF model seems to capture the fundamental physics of monovalent and divalent cation hydration, but is in serious error for describing the free energy of aqueous solvation of monovalent and multivalent anions.

## THE ELECTRONIC REACTION FIELD (ERF) MODEL

The principal issue to address is confining the solute wave function (or charge density) to a specified molecular cavity. In related areas, the model problem of the hydrogen atom confined in a sphere has been solved exactly, and approximate calculations of larger atoms confined within spheres have been performed in connection with estimating pressure effects on the electronic structure and properties of atoms.<sup>26,27</sup> These calculations, while not sophisticated by current electronic structure standards, do demonstrate the feasibility of wave function confinement, at least for simple cavity geometries.

Total wave function containment can be achieved either by explicit imposition of this condition in a constrained optimization sense, or by expansion of the wave function (or charge density) in terms of a set of basis functions all of which individually satisfy this boundary condition. The latter approach is simpler and more feasible for spherical ions, and is what we shall use in this exploratory study. The standard atom-centered Gaussian basis functions of quantum chemistry are not directly appropriate for finding a wave function constrained to a cavity because they do not have sharply defined extent. Instead, they have tails that decay into the dielectric continuum. We require modified functions that go exactly to zero at the boundary, with nonzero derivatives at the boundary.<sup>26,27</sup> Hence simply scaling Gaussian exponents, or shifting the centers of functions such that they approach zero at the boundary to within a prescribed tolerance is inadequate, because all derivatives of such functions approach zero at the boundary. Hence calculations will yield an energy that is substantially too high. To state it more strongly, a set of such functions can never approach completeness for this problem.

The question then is how to modify the standard Gaussian basis functions of gas phase electronic structure theory to describe confinement. We use a modulating function such

that the original Gaussian vanishes identically at the boundary:

$$f' = s \cdot f, \quad (2)$$

where  $s$  is the modulating function that satisfies the boundary condition, and depends only on the atomic radial coordinate,  $r$ , and  $f$  is the original Gaussian function. We have explored the modulation function

$$s = \left[ 1 - \left( \frac{r}{a} \right)^n \right], \quad (3)$$

where the parameter  $a$  is the optimizable radius associated with the atom. A set of modulated basis functions based on Eqs. (2) and (3) can approach completeness because their gradients and higher derivatives at the boundary are nonvanishing, as the boundary condition allows. They also have the desirable property of reducing to the gas-phase functions smoothly as the atomic radii approach infinity.

The primary technical difficulty to be overcome with the use of the modulated basis functions is the fact that they have nonzero amplitude beyond the cavity boundary, while all quantum mechanical matrix elements must now be defined only over the cavity volume. The typical Gaussian integral machinery that makes the unmodulated functions appealing for gas phase calculations is predicated on performing integrals over all space. We therefore use adaptive numerical integration for evaluating all one- and two-matrix elements over the cavity volume, and not over the nonzero tails that extend beyond. We exploit spherical symmetry so that the angular pieces are determined analytically, and only the one-dimensional radial components are evaluated numerically.

The reaction field potential [Eq. (1)] is then added to the self-consistent field equations of Hartree–Fock theory. Iteration of the equations via standard gas-phase procedures leads to an updated solute charge density (trivially a monopole in the case of atomic ions) that in turn modifies the reaction field. In this way self-consistency will be obtained between the electronic wave function, and the reaction field due to solvation.

We do not know how standard Gaussian basis sets will perform under wave function confinement. We therefore use the even-tempered basis functions derived in Ref. 28. The even-tempered basis functions are systematic sequences of Gaussian primitives, which can approach completeness.<sup>28</sup> The radial functions are

$$R_{kl}(r) = N_l(\zeta_{kl}) e^{-\zeta_{kl} r^2}, \quad (4)$$

where the parameters,  $\zeta_{kl}$ , for a given value of  $l$  are determined according to

$$\zeta_{kl} = \alpha_l \beta_l^k, \quad k = 1, 2, \dots, N_l. \quad (5)$$

The parameters  $\alpha_l$ , and  $\beta_l$  were optimally determined for all atoms through argon.<sup>28</sup> Two additional points in regard to these basis sets should be noted. Since each sequence of primitive Gaussians was optimized for the atom,<sup>28</sup> it is not optimally suitable for the anion. The addition of an electron should result in greater electron–electron repulsion, and therefore we expect the wave function of the anion to be more diffuse than that of atom, and the basis sets should be

TABLE I. Dependence of optimized radius of  $F^-$  as a function of basis set size and Gaussian function modulation.

Radius (Å)	6s/3p 3 diffuse linear	8s/4p 3 diffuse linear	10s/5p 3 diffuse linear	14s/7p 3 diffuse linear	6s/3p 3 diffuse quadratic	8s/4p 3 diffuse quadratic	10s/5p 3 diffuse quadratic	14s/7p 3 diffuse quadratic
2.25	-99.316 00	-99.478 52			-99.276 78	-99.450 84	-99.513 83	
2.35	-99.319 48	-99.484 41			-99.280 62	-99.452 36	-99.520 16	
2.45	-99.320 53	-99.487 85			-99.282 02	-99.451 03	-99.524 02	
2.55		-99.489 57	-99.528 86	-99.540 54	-99.281 180		-99.526 15	-99.529 67
2.65			-99.529 71	-99.541 00			-99.527 04	-99.540 90
2.75							-99.527 05	-99.540 98

supplemented with additional diffuse functions. These additional Gaussian functions can be determined by extending the  $\zeta_{kl}$  to negative  $k$  values. Second, since optimal  $\alpha$  and  $\beta$  values were not determined for atoms beyond argon, the basis set for the potassium cation is not optimal.

## RESULTS

Table I shows the convergence of cavity radius for the fluoride anion, as a function of the size of the even-tempered basis set, and as a function of the modulation exponent in Eq. (3), i.e., the power dependence on  $r/a$  which describes how rapidly the Gaussian function decays to zero at the boundary. The primary conclusion to be drawn from Table I is that beyond the 8s/4p basis, the optimized radius does seem to converge to a stable value, and that little difference in converged radius is found for either linear or quadratic modulation. Therefore for all ERF calculations performed for anions and cations, we used the largest basis for which optimal  $\alpha$  and  $\beta$  parameters were defined in the original paper on even-tempered basis sets.<sup>28</sup> For all ERF calculations on anions, three additional diffuse functions were defined. We used linear modulation in all subsequent calculations.

Figure 1 shows the total free energy using the ERF model for the monovalent and divalent cations  $Li^+$ ,  $Na^+$ ,  $K^+$ , and  $Mg^{2+}$ . Figure 2 shows the total free energy using the ERF model for the monovalent and divalent anions  $F^-$ ,  $Cl^-$ , and  $S^{2-}$ . These free energy curves for each ion are relative energies with respect to the minimum in the combined Hartree-Fock energy with wave function totally confined plus the Born free energy term [Eq. (1)]. The minimum in the total combined energy corresponds to the optimized

Born radius for each ion. We also plot the cavitation free energy as a function of radius, values that can be determined from the probability of a given cavity size occurring in the neat water liquid,<sup>29</sup> for which reasonable statistical significance is found for cavities up to roughly 4.0 Å.<sup>30</sup> Note that the energy scales plotted are different between cations and anions; cations experience a greater repulsion when squeezed and we return to this point later.

Tables II and III summarize our results for cations and anions, respectively, using the ERF model. The entries in each table include the even-tempered basis set size used, the absolute minimized value of the sum of the ERF energy, the experimental hydration free energy, enthalpy, and entropy ( $-T\Delta S$ ),<sup>31</sup> and the predicted solvation energy from the ERF model, taken to be the difference in the ERF energy and the energy of the unconfined atom ( $a \rightarrow \infty$ ). Overall the experimentally determined entropic contribution at room temperature is small, and the free energy is dominated by the enthalpic term. However, for quantitative comparisons the room temperature entropy is still roughly 5%–10% of the free energy. We will compare our ERF model energy to both the experimentally reported  $\Delta G_{hyd}$  and  $\Delta H_{hyd}$ .

We also list reported optimal ion radii by Rashin and Honig<sup>32</sup> determined from the Born expression using the enthalpy of solvation taken from experimental measurements, as well as converged radii at the ERF minimum energy, and ERF model radii corrected for the cavity work to create a spherical cavity of a given size in water. We also note that the converged radius in our ERF model for the potassium ion is  $\sim 2.5$  Å using the (nonoptimal) 16s/8p even-tempered basis for argon. Using a basis set approaching completeness we found that the optimized cavity radius decreases to 2.3 Å.<sup>33</sup>

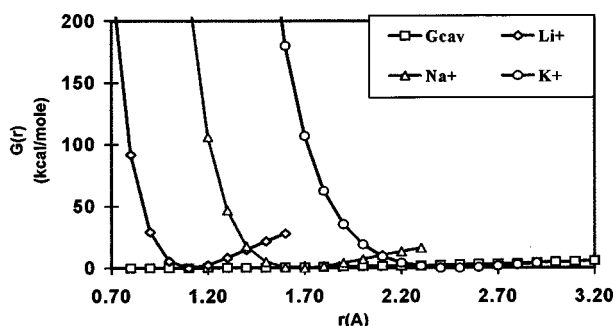


FIG. 1. The total ERF+Born energy for monovalent cations as a function of radius:  $Li^+$  (diamonds),  $Na^+$  (triangles), and  $K^+$  (circles). Also plotted is the free energy work of creating a cavity in water as a function of radius (Ref. 32) (squares).

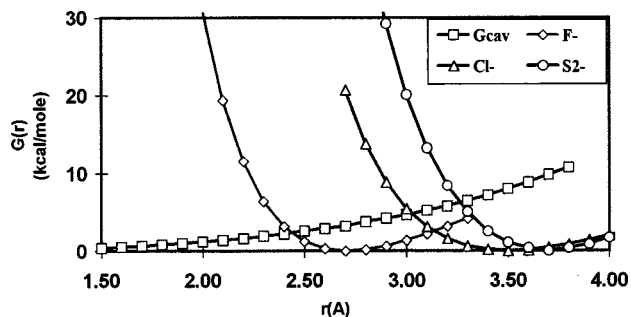


FIG. 2. The total ERF+Born energy for anions as a function of radius:  $F^-$  (diamonds),  $Cl^-$  (triangles), and  $S^{2-}$  (circles). Also plotted is the free energy work of creating a cavity in water as a function of radius (Ref. 32) (squares).

TABLE II. Comparisons with and summary of the ERF model for cations.

Cation	Li <sup>+</sup>	Mg <sup>2+</sup>	Na <sup>+</sup>	K <sup>+</sup>
Basis set <sup>a,b</sup>	16s/0 diffuse	16s/8p/0 diffuse	16s/8p/0 diffuse	16s/8p/0 diffuse
ERF energy at optimal radius (hartrees)	-7.443 503 6	-199.609 79	-161.813 33	-599.051 84
$\Delta G_{\text{hyd}}$ (kcal/mol) <sup>c</sup>	-113.5	-437.4	-87.2	-70.5
$\Delta H_{\text{hyd}}$ (kcal/mol) <sup>c</sup>	-125.8	-462.4	-98.5	-78.4
$-T\Delta S_{\text{hyd}}$ (kcal/mol) <sup>c</sup>	11.5	24.9	9.3	6.6
$\Delta E = E(\text{solution}) - E(\text{vacuum})$ (kcal/mol)	-131.1	-490.0	-86.6	-53.0
Born radius (Å) <sup>d</sup>	1.22	1.35	1.56	2.02
ERF radius (Å)	1.1	1.2	1.7	2.5
ERF+cavity work radius (Å) <sup>e</sup>	1.1	1.2	1.7	2.4

<sup>a</sup>Basis is not defined for potassium in Ref. (28), and results are nonoptimal.<sup>b</sup>Reference 28.<sup>c</sup>Reference 31.<sup>d</sup>Reference 32.<sup>e</sup>Reference 30.

It can be seen from Tables II and III that the ERF model predicts the “Born radii” for cations with reasonable accuracy, while the ERF model differs from the Born radii for anions by a factor of 2. Of course the Born radius is not an experimental observable. We are merely emphasizing that the radius is an optimizable quantity in our model, whose value for cations *predicted* from the ERF model is consistent with a fitting protocol where the radius is treated as an adjustable parameter.<sup>32</sup> More important, the cation solvation energies predicted from the ERF model seem to be in good agreement with experimental solvation enthalpies, with differences on the order of  $\sim 5\%$ . This very good qualitative agreement with our predicted radii and the Born radii arrived at parametrically, and with energies from experiment, is confirmation that the fundamental physics of solvation is captured remarkably well by the ERF/Born theory for positively charged ions. As seen in Fig. 1, the work of cavity formation ( $\Delta G_2$ ) is relatively flat throughout cavity sizes 0.8–2.5 Å.<sup>30</sup> The dominating effect for cations seems to be the manifestation of the Pauli exclusion principle, i.e., the rapid rise in energy as the confined cavity radius is made smaller than the optimal radius. Since the Born terms do not provide an equal or more rapid rate of free energy stabilization with decreasing radius, the optimized radius and dielectric boundary is

largely determined by the volume that a cation can occupy. We would expect that the free energy due to solvent molecular reorganization and non-Born terms ( $\Delta G_4$ ) will also not effectively compete with this rapid rise in kinetic energy at smaller radii either.

We see that anions occupy larger cavities than cations for a given isoelectronic pair, and the ERF optimized energy severely underestimates the experimental free energy or enthalpy of solvation. The likely reason for the mismatch is that the Born theory breaks down for anions. The cavitation term is now more significant and unfavorable, beginning to rise for cavity sizes of 2.5–4.0 Å that are relevant for anions, and though the corrections in optimized radii due to  $\Delta G_2$  are still small, they are significant enough to decrease the optimal radius between 0.1 and 0.2 Å. However, we expect  $\Delta G_4$  to be more significant, since the solvent structural reorganization around a negatively charged sphere will present a greatly reduced electron density due to unshielded hydrogens pointing toward the anion, providing for significant free energy stabilization at smaller cavities. Furthermore, given the much less steep rise in energy as anions are confined to smaller and smaller cavities suggests that the non-Born terms can provide a competitive free energy to stabilize smaller cavities. In the case of anions, it is the molecular nature of

TABLE III. Comparisons with and summary of the ERF model for anions.

Anion	F <sup>-</sup>	Cl <sup>-</sup>	S <sup>2-</sup>
Basis set <sup>a</sup>	14s/7p/3 diffuse	16s/8p/3 diffuse	16s/8p/3 diffuse
ERF energy at optimal radius (hartrees)	-99.541 003	-459.623 46	-397.551 18
$\Delta G_{\text{hyd}}$ (kcal/mol) <sup>b</sup>	-111.1	-81.3	-314.3
$\Delta H_{\text{hyd}}$ (kcal/mol) <sup>b</sup>	-121.9	-87.2	-321.5
$-T\Delta S_{\text{hyd}}$ (kcal/mol) <sup>b</sup>	11.1	6.7	10.0
$\Delta E = E(\text{solution}) - E(\text{vacuum})$ (kcal/mol)	-52.0	-43.2	-118.1
Born radius (Å) <sup>c</sup>	1.32	1.80	1.83
ERF radius (Å)	2.7	3.5	3.7
ERF+cavity work radius (Å) <sup>d</sup>	2.6	3.3	3.5

<sup>a</sup>Reference 28.<sup>b</sup>Reference 31.<sup>c</sup>Reference 32.<sup>d</sup>Reference 30.



aqueous solvent that determines the anion radius, physics that is not captured in the Born model.

## CONCLUSIONS

The very literal interpretation of the Born reaction field expression for ions in the context of electronic structure calculations requires zero overlap of the quantum mechanical wave function of the solute and the solvent, which permits the latter to be treated as a classical dielectric. This allows us to determine a radius for which there is an optimal balance between the cost of wave function confinement and the Born free energy of solvation. This lifts the empiricism of defining a Born radius for cations and anions, and allows them to be predicted directly from Born theory in the context of electronic structure calculations. This more rigorous treatment of the Born theory for ion solvation allows us to determine the merit of this simplest reaction field approach.

In the case of aqueous solvation of monovalent and divalent cations, the free energy of solvation is dominated by the reaction field electrostatics and steric effects of the surrounding solvent. The approximation of total wave function containment perhaps mimics the higher electron density of oxygens oriented toward the cation, thereby not permitting great penetration of the solute wave function into the solvent. Therefore the dielectric boundary is largely defined by the Pauli exclusion principle of the cation itself, i.e., how much it can be squeezed and still gain reaction field energy stabilization. Little of the molecular nature of water solvent is energetically competitive at these small radii, i.e.,  $\Delta G_2$  is absolutely small and likely  $\Delta G_4$  is also relatively small, and therefore the Born expression seems to be largely correct for cations.

By contrast, the physics of anion solvation is not adequately described by the Born theory since the effects arising from the molecular nature of aqueous solvent matter in this case. In particular,  $\Delta G_4$  is probably significant at smaller cavity sizes due to a molecular reorganization of water molecules that present their hydrogens toward the anion, or equivalently a greatly diminished electron density at the anion boundary that makes total wave function confinement less reasonable. In fact anions are larger than cations for a given isoelectronic pair, and it is the molecular nature of solvent or the non-Born terms that provide significant stabilization at smaller radii. Therefore, the protocols developed to determine a Born radius for anions are a sensible parametric means for correcting for solvent molecular effects, and non-linear terms that are not captured in Born theory.

## ACKNOWLEDGMENTS

C.P.H. acknowledges a postdoctoral fellowship from the Miller Institute for Basic Research in Science. We gratefully acknowledge support from the Air Force Office of Sponsored Research, Grant No. FQ8671-9601129, and the National Energy Research Supercomputer Center for computer time, and thank L. Pratt for use of the cavity work data.<sup>30</sup>

- <sup>1</sup>J. Tomasi and M. Persico, *Chem. Rev.* **94**, 2027 (1994).
- <sup>2</sup>M. W. Wong, K. B. Wiberg, and M. J. Frisch, *J. Am. Chem. Soc.* **114**, 1645 (1992).
- <sup>3</sup>C. J. Cramer and D. G. Truhlar, *J. Am. Chem. Soc.* **115**, 8810 (1993).
- <sup>4</sup>C. J. Cramer and D. G. Truhlar, *J. Am. Chem. Soc.* **113**, 8552 (1991).
- <sup>5</sup>R. R. Pappalardo, E. S. Marcos, M. F. Ruiz-Lopez, D. Rinaldi, and J.-L. Rivail, *J. Am. Chem. Soc.* **115**, 3722 (1993).
- <sup>6</sup>R. Bianco, S. Miertus, M. Persico, and J. Tomasi, *Chem. Phys.* **168**, 281 (1992).
- <sup>7</sup>M. W. Wong, K. B. Wiberg, and M. J. Frisch, *J. Am. Chem. Soc.* **114**, 523 (1992).
- <sup>8</sup>W. M. Latimer, K. S. Pitzer, and C. M. Slansky, *J. Chem. Phys.* **7**, 108 (1939).
- <sup>9</sup>K. V. Mikkelsen, Y. Luo, H. Agren, and P. Jorgensen, *J. Chem. Phys.* **100**, 8240 (1994).
- <sup>10</sup>K. Laasonen and M. L. Klein, *J. Am. Chem. Soc.* **116**, 11620 (1994).
- <sup>11</sup>M. Tuckerman, K. Laasonen, M. Sprik, and M. Parrinello, *J. Chem. Phys.* **103**, 150 (1995).
- <sup>12</sup>K. Baldridge and A. Klamt, *J. Chem. Phys.* **106**, 6622 (1997).
- <sup>13</sup>T. Fox, N. Rosch, and R. J. Zauhar, *J. Comput. Chem.* **14**, 253 (1993).
- <sup>14</sup>R. J. Hall, M. M. Davidson, N. A. Burton, and I. H. Hillier, *J. Phys. Chem.* **99**, 921 (1995).
- <sup>15</sup>A. A. Rashin, M. A. Bukatin, J. Andzelm, and A. T. Hagler, *Biophys. Chem.* **51**, 375 (1994).
- <sup>16</sup>A. Fortunelli and J. Tomasi, *Chem. Phys. Lett.* **231**, 34 (1994).
- <sup>17</sup>D. J. Tannor, B. Marten, R. Murphy, R. A. Friesner, D. Sitkoff, A. Nicholls, M. Ringnalda, W. A. Goddard III, and B. Honig, *J. Am. Chem. Soc.* **116**, 11875 (1994).
- <sup>18</sup>K. V. Mikkelsen, P. Jorgensen, and H. J. A. Jensen, *J. Chem. Phys.* **100**, 6597 (1994).
- <sup>19</sup>D. Chipman, *J. Chem. Phys.* **110**, 1611 (1999).
- <sup>20</sup>Y. P. Liu and M. D. Newton, *J. Phys. Chem.* **99**, 12382 (1995).
- <sup>21</sup>C. J. Cramer and D. G. Truhlar, *Science* **256**, 213 (1992).
- <sup>22</sup>D. J. Giesen, C. J. Cramer, and D. G. Truhlar, *J. Phys. Chem.* **99**, 7137 (1995).
- <sup>23</sup>W. C. Still, A. Tempczyk, R. C. Hawley, and T. Hendrickson, *J. Am. Chem. Soc.* **112**, 6127 (1990).
- <sup>24</sup>M. Born, *Z. Phys.* **1**, 45 (1920).
- <sup>25</sup>R. Cammiand and J. Tomasi, *J. Chem. Phys.* **100**, 7495 (1994).
- <sup>26</sup>D. Suryanarayana and J. A. Weil, *J. Chem. Phys.* **64**, 510 (1976).
- <sup>27</sup>E. V. Ludena, *J. Chem. Phys.* **69**, 1770 (1978).
- <sup>28</sup>M. W. Schmidt and K. Rudenberg, *J. Chem. Phys.* **71**, 3951 (1979).
- <sup>29</sup>H. Reiss, H. L. Frisch, and J. L. Lebowitz, *J. Chem. Phys.* **31**, 369 (1959).
- <sup>30</sup>A. Pohorille and L. R. Pratt, *J. Am. Chem. Soc.* **112**, 5066 (1990).
- <sup>31</sup>Y. Marcus, *Biophys. Chem.* **51**, 111 (1994).
- <sup>32</sup>A. A. Rashin and B. Honig, *J. Phys. Chem.* **89**, 5588 (1985).
- <sup>33</sup>Unpublished results.